REMARKS/ARGUMENTS

Claims 17-52 and new claims 53-57 are pending in this Application. The Office Action mailed on June 2, 2005, includes the following rejections:

1. Claims 17-52 are rejected under 35 U.S.C. § 112 first paragraph.
2. Claims 17-52 are rejected under 35 U.S.C. § 112 second paragraph.

Applicant respectfully addresses the basis for each of the Examiner's rejections below.

Claim Rejections – Claims 17-52 are rejected under 35 U.S.C. 112 first paragraph as failing to comply with the enablement requirement.

Applicant submits that the specification as file is enabled to support claims 17-52 and new claims 53-57 and fully complies with 35 U.S.C. § 112 first paragraph. Specifically, a working example is provided in the form of a human patient that was treated in accordance with the present invention. The skilled artisan with recognize the rarity with which such a human patient is encountered that is still living. The human patient example provides in vivo support, enablement and a working example that supports the well-known and widely-recognized model system using cells in vitro. Therefore, it is simply inconceivable that not a single claim in the present application is allowable based on the clear limitations found in the independent and the dependent claims. For example, specific claims denote the exact caloric requirements that would be provided to a patient based on the examples provided in the specification.

In order to make a rejection under 35 U.S.C. § 112 first paragraph, the Examiner has the initial burden to establish a reasonable basis to question the enablement provided for the claimed invention, e.g., *In re Wright*, 999 F.2d 1557, 1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993) states the Examiner must provide a reasonable explanation as to why the scope of protection provided by a claim is not adequately enabled by the disclosure. A specification that contains a teaching of the manner and process of making and using an invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented must be taken as being in compliance with the enablement requirement of 35 U.S.C. 112, first

paragraph, unless there is a reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support. No such reasonable doubt of the objective truth, or for that matter, the objective examples, is supported by the mere listing of the *Wands* factors in the action.

The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. *In re Angstadt*, 537 F.2d 498, 504, 190 USPQ 214, 219 (CCPA 1976). The present application provides *inter alia* both *in vitro* and *in vivo* examples and given the scope of the disclosure, IF any experimentation would be necessary such experimentation would clearly not be undue. Furthermore, a detailed procedure for making and using the invention may not be necessary if the description of the invention itself is sufficient to permit those skilled in the art to make and use the invention. The present application provides more that adequate support to enable the SKILLED artisan to make and use the present invention.

The Action fails to meet its initial burden to provide specific findings of fact that are supported by the evidence to establish a reasonable basis to question the enablement provided for the claimed invention, e.g., see *In re Wright*, 999 F.2d 1557, 1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993). As listed hereinbelow, the Action's initial burden is rebutted for each and every reason for rejection by the following listed examples of support in the present application:

1) Detailed examples of using a seven carbon fatty acid and substituted, unsaturated or branched heptanoates can be used in addition to other modified seven-carbon fatty acids ([0070]).

2) Numerous specific compounds that can be used in the present invention, e.g., seven-carbon fatty acid composition include n-heptanoic acid, triglyceride having an n-heptanoic acid, triheptanoin, a substituted carbon fatty acid composition, unsaturated carbon fatty acid composition, branched seven-carbon fatty acid composition, 4-methylhexanoate, 4-methylhexenoate, 3-hydroxy-4-methylhexanoate; 5-methylhexanoate, 5-methyhexenoate and 3-hydroxy- 5 - methylhexanoate.

3) Examples of the type of cardiac disorder that can be treated, e.g., cardiac muscle weakness and cardiac myopathy.

4) Specific examples of *in vitro* treatments in the form of well-known, characteristics and generally accepted *in vitro* systems, e.g., cell culture examples using human cells (see e.g., [0089]).

5) Specific examples of *in vivo* treatments in the form of and an *in vivo* example of treating a living infant (see e.g., [0089]).

6) Dosage ranges for treatment are also provided, e.g., between about 15 and about 40% of the daily dietary caloric requirement for the patient.

7) Methods of administering, e.g., enteral administering.

Below is the text from the application as filed that clearly supports the studies and the claims as filed. Briefly, cells are taken from a deceased patient and treated with the present invention thereby allowing the cells to survive. Next, cells from the deceased patient's unborn sibling were obtained, determined to have the same enzymatic deficiency and also treated, successfully, using the present invention. It is not clear what other, scientifically valid examples, the Office wishes the Applicant to present. Clearly, the seven carbon fatty acid was able to overcome the genetic deficiency in these cells. Finally, the second patient, once born, was successfully treated and discharged without meeting the fate of its sibling.

[0080] The addition of n-heptanoic acid to cultured cells (fibroblasts) taken from patients with a lethal form of translocase deficiency indicated successful oxidation.

[0081] Because a sibling had died at the age of four days from severe translocase deficiency, amniocytes obtained from a fetus were examined for competency in fatty acid metabolism. The tests revealed that the fetus also had severe translocase deficiency.

[0082] Fibroblasts taken from the deceased sibling and amniocytes taken from the fetus were both evaluated for fatty acid metabolism of n-heptanoic acid (C7) using a tandem mass spectrometry assay previously reported. (Yang, et al. 1998. "Identification of four novel mutations in patients with carnitine palmitoyltransferase II (CPT II) deficiency," Mol Genet Metab 64:229-236). The mass spectrometry results are presented for palmitate in Fig. 3A and triheptanoin in Fig. 3B for the fibroblasts taken from the deceased sibling, and for palmitate in Fig. 4A and triheptanoin in Fig. 4B for the amniocytes taken from the fetus. Results of the study showed that n-heptanoic acid (Fig. 3B and 4B) was independent of carnitine/acylcarnitine translocase and readily oxidized to propionyl-CoA despite the translocase deficiency in both cell lines. Based on the successful metabolism of n-heptanoic acid by the two cell lines having severe translocase deficiency, the tandem mass spectrometry assay was performed on fibroblast cell lines taken from normal patients and from patients affected by the following inherited defects of fat oxidation as proven by direct enzyme assay in other collaborating laboratories: carnitine palmitoyltransferase I (CPT I); severe carnitine/acyl carnitine translocase (TRANSLOCASE); carnitine palmitoyltransferase II (CPT II); the "cardiac" form of very-long-chain acyl-CoA dehydrogenase (VLCAD-C); the "hypoglycemic" form of very-long-chain acyl-CoA dehydrogenase (VLCAD-H); the mitochondrial trifunctional protein (TRIFUNCTIONAL); long-chain L-3-hydroxy-acyl-

CoA dehydrogenase (LCHAD); medium-chain acyl-CoA dehydrogenase (MCAD); short-chain acyl-CoA dehydrogenase (SCAD); electron transfer flavoprotein QO dehydrogenase-mild (ETF-DH mild); and electron transfer flavoprotein QO dehydrogenase-severe (ETF-DH severe). Each cell line was incubated separately with 7-2H3-heptanoate (D3-C7), 8-2H3-octanoate (D3-C8), 9-2H3-nonanoate (D3-C9), and 16-2H3-palmitate (D3-C16). The results are given as tandem mass spectrometry in Fig. 5A-L for D3-C7; Fig. 6A-L for D3-C8; Fig. 7A-L for D3-C9; and Fig. 8A-L for D3-C16.

Support for the treatment of cardiac cells, conditions and the like is provided by the data in Fig. 5E, which is a graph depicting a tandem mass spectrometry profile for fibroblasts treated with D3-C7 (7-$^{2}H_{3}$-heptanoate), which were obtained from a child who suffered from the "cardiac" form of very-long-chain acyl-CoA dehydrogenase (VLCAD-C) deficiency. Again, the Applicants inquire what additional data the Office is requesting as the specification clearly supports the use of the odd-chain fatty acids to treat the "cardiac" form of very-long-chain acyl-CoA dehydrogenase (VLCAD-C) deficiency.

Therefore, the present application provides complete support to enable the skilled artisan to make and use the present invention. The application provides detailed, working examples of using a seven carbon fatty acid compounds, working examples of the disorders that can be treated, how the compounds can be administer, what dosage ranges can be administer and supports this with not only *in vitro* examples, but ACTUAL *in vivo* treatments of an ACTUAL living and breathing patient. All the information necessary to make and use the present invention is provided in either the application itself or the knowledge of the skilled artisan.

As stated by the court, "it is incumbent upon the Patent Office, whenever a rejection on this basis is made, to explain *why* it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement. Otherwise, there would be no need for the applicant to go to the trouble and expense of supporting his presumptively accurate disclosure." *In re Marzocchi*, 439 F.2d 220, 224, 169 USPQ 367, 370 (CCPA 1971). The Action provides mere conclusory statements to support the position that the application is not enabled and as such the Action does not meet the standard necessary to establish a lack of enablement. The Action FAILS to back up the assertions with acceptable evidence or reasoning.

Applicants hereby request that the Examiner state for the record the specific reasons, e.g., information about one or more missing essential parts or relationships between parts that one skilled in the art could not develop without undue experimentation, that would not allow the person of ordinary skill in the art to make or use the present invention, or withdraw the rejection.

Furthermore, it is not necessary for the application to disclose every know aspect of the invention. The application is not required to provide, and preferably omits, information that would be known to the skilled artisan, e.g., see *In re Buchner*, 929 F.2d 660, 661, 18 USPQ2d 1331, 1332 (Fed. Cir. 1991); *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1384, 231 USPQ 81, 94 (Fed. Cir. 1986), *cert. denied*, 480 U.S. 947 (1987); and *Lindemann Maschinenfabrik GMBH v. American Hoist & Derrick Co.*, 730 F.2d 1452, 1463, 221 USPQ 481, 489 (Fed. Cir. 1984). As the skill artisan includes PhDs, MSs, MDs, pharmacists and compounders and even-chain fatty acids have been studied for many decades, the skill and knowledge in the field is high. The application need only provide the person of ordinary skill in the art to make or use the present invention, which the present application clearly meets by the examples listed above. Compliance with the enablement requirement of 35 U.S.C. 112, first paragraph, does not turn on whether an example is disclosed. However, the present application provides both "working examples" of treatments to a patient and "prophetic examples." The present Applicant more that adequately enables the present invention by providing detailed examples of the compounds, amounts of the compounds, precise ranges for the caloric percentages, examples of the disorder that can be treated, how the compounds can be administered, what dosage ranges can be used and supports this with not only *in vitro* examples, but ACTUAL *in vivo* treatments of an ACTUAL living and breathing patient.

It is not necessary that an applicant have actually reduced the invention to practice prior to filing, e.g., see *Gould v. Quigg*, 822 F.2d 1074, 1078, 3 USPQ 2d 1302, 1304 (Fed. Cir. 1987). Yet, the present application provides not only *in vitro* examples, but ACTUAL *in vivo* treatments of an ACTUAL living and breathing patient.

It is not necessary for the Applicant to "enable one of ordinary skill in the art to make and use a perfected, commercially viable embodiment absent a claim limitation to that effect." *CFMT, Inc. v. Yieldup Int'l Corp.*, 349 F.3d 1333, 1338, 68 USPQ2d 1940, 1944 (Fed. Cir. 2003). Yet again, the present application provides examples of actual treatments of a living and breathing patient.

Furthermore, the MPEP (e.g., MPEP § 2164) states that even a single working example in the specification for a claimed invention is enough to preclude a rejection which states that nothing is enabled since at least that embodiment would be enabled. The presence of only one working example should never be the sole reason for rejecting claims as being broader than the enabling disclosure, even though it is a factor to be considered along with all the other factors. To make a valid rejection, one must evaluate all the facts and evidence and state why one would not expect to be able to extrapolate that one example across the entire scope of the claims. The Action fails to accomplish this requirement and the argument above clearly rebuts any initial shift in the burden from the Office to the Applicant.

As such, the specification satisfies the written description requirement under 35 U.S.C. § 112, first paragraph. For the reasons mentioned above, the Applicant respectfully requests the Examiner withdraw the rejection under 35 U.S.C. § 112.

Claim Rejections – Claims 17and 46 are rejected under 35 U.S.C. 112 second paragraph.

The action states that claims 27 and 42 are indefinite as the claims do not recite the parameters of what an effective amount is or how relief may be measured.

Applicant submits that the claims are not indefinite and comply with 35 U.S.C. § 112 second paragraph. It is not necessary for the application to state specifically what the exact amount to be administered to each and every patient, as that is within the scope of the knowledge of the skilled artisan. Since a statement of utility in the specification contains within it a connotation of how to use the present invention and the art recognizes that standard modes of administration are known and contemplated, 35 U.S.C. 112 is satisfied, e.g., see *In re Johnson*, 282 F.2d 370, 373, 127 USPQ 216, 219 (CCPA 1960); *In re Hitchings*, 342 F.2d 80, 87,

144 USPQ 637, 643 (CCPA 1965). See also *In re Brana*, 51 F.2d 1560, 1566, 34 USPQ2d 1437, 1441 (Fed. Cir. 1993). Specifically, it is not necessary to specify the dosage or how relief may be measured as it is known to one skilled in the art and such information can be obtained without undue experimentation. One skilled in the art, based on knowledge of compounds and treatments having similar physiological or biological activity, would be able to discern an appropriate dosage or how relief may be measured without undue experimentation, and as such is sufficient to satisfy 35 U.S.C. 112. Therefore, Applicant submits that the claims are not indefinite.

As such, the claims are not indefinite and comply with 35 U.S.C. § 112, second paragraph. For the reasons mentioned above, the Applicant respectfully requests the Examiner withdraw the rejection under 35 U.S.C. § 112 second paragraph.

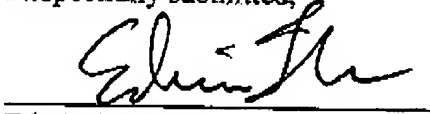
Conclusion

Claims 17-52 and new claims 53-57 are pending in the present application. New claims 53-57 find support throughout the application, specifically the original claims 17-52. In light of the remarks and arguments presented above, Applicant respectfully submits that the claims in the application are in condition for allowance. Favorable consideration and allowance of the pending claims 17-57 are therefore respectfully requested.

If the Examiner has any questions or comments, or if further clarification is required, it is requested that the Examiner contact the undersigned at the telephone number listed below.

Dated: April 17, 2006.

Respectfully submitted,



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